Research Article

Age at Sexual Debut as a Determinant of HPV Infection in Women with Clinically Normal Cervix in Indonesia

Tofan Widya Utami[1], Laila Nuranna, Gatot Purwoto[1], Junita Indarti[2], Najmarani Devi Firdaus[1], Arisda Oktalia[1], Nuni Sulastri[1], Aria Kekalih[3]

[1]Division of Gynecology Oncology Departments of Obstetrics and Gynecology
[2]Division of Social Obstetrics and Gynecology
Departments of Obstetrics and Gynecology
[3]Department of Community Medicine
Faculty of Medicine Universitas Indonesia
Jakarta

Abstract

Objective: This study examined the association between sexual debut and HPV infection in Indonesian women with a clinically normal cervix, contextualized within the Sustainable Development Goals (SDGs).

Methods: This prospective cohort study utilized primary data from structured interviews and gynecological exams conducted by the Female Cancer Program (FCP) team across public and private health providers in Jakarta (January 2012–July 2018) of clinically normal cervix subjects from VIA test. Cervical cancer–related data were collected including age at sexual debut and HPV DNA results. HPV DNA testing using the HPV Xpress Matrix kit, with genotyping by PCR (SPF10-DEIA-LiPA25). Early sexual debut (≤18 years) was reported in 17.7% of participants. In both univariate and multivariate logistic regression, no examined factors including age group, early sexual debut, smoking history, marital status, contraception use, or menarche were significantly associated with HPV infection. Early sexual debut showed no meaningful association with HPV positivity (adjusted OR 0.981; 95% CI 0.491–1.882; p = 0.908).

Conclusion: Early sexual debut was not significantly associated with HPV infection in women with a clinically normal cervix. Nevertheless, integration of HPV prevention, SRH education, and early screening initiatives remains pivotal to achieving SDG 3.7 and 5.6 targets in Indonesia.

Keywords: cervical cancer, HPV infection, negative VIA, sexual debut, Sustainable Development Goals.

Correspondence author. Tofan Widya Utami. Gynecology Oncology Division, Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Indonesia, Jakarta, Email: tofanwidya@yahoo.com Telephone : +62 818 0869 6983

INTRODUCTION

Cervical cancer is a common type of cancer and a cause of death among women worldwide.[1] Persistent infection with a high-risk type of human papilloma virus (Hr-HPV) has been proved to be a significant cause of cervical cancer. The lifetime risk of sexually active women being infected with at least one type of human papillomavirus (HPV) is relatively high, at more than 50% and up to 80%.[2]

Women who experience cervical cancer often occur at the age of 30-40 years and over. The risk factors for a person being infected with HPV in the cervix are: sexual activities at early age, frequent change of sexual partners, sexually transmitted infections, family history of cervical cancer, smoking, immunosuppression.[3] Sexual and Reproductive Health (SRH) plays a crucial role in the transmission of HPV. Certain SRH-related behaviors, such as early sexual initiation and the number of sexual partners, have been associated with an increased risk of HPV, ultimately contributing to a higher likelihood of cervical cancer.[4] Sexual debut earlier than 18 old might increase the risk of becoming cervical cancer by 2.95 times than women who began sexual intercourse later in life.[5] However, the relationship between early sexual debut and HPV infection has not been consistently documented

in the literature, particularly in Indonesia. This gap in evidence raises the question of whether Indonesia exhibits a similar pattern in the association between age at sexual debut and HPV infection. Understanding this association could have significant implications for future cervical cancer screening regulations and preventive education in Indonesia.

Sustainable development goals (SDGs) are targets for all developed and developing countries to achieve by 2030. SDGs related to sexual and reproductive health consist of the goals of good health and well-being (SDG 3) and also gender equality (SDG 5).[6] This study aimed to determine the associations of sexual debut and marital status with HPV infection in women with a clinically normal cervix in Indonesian population and discuss it from the SDGs point of views.

METHODS

This prospective cohort study included primary data by consecutively sampling all patients who came to Primary Health Care (PHC) facilities and other health care facilities enrolled in the *"See and Treat"* Female Cancer Program (FCP) Jakarta and from the private clinics of the Obstetrics and Gynecology Department of Dr. Cipto Mangunkusumo National General Hospital (RSCM) in Indonesia from January 2012 to July 2018. Sampling process was done by FCP team comprises midwives, general practitioners, obstetricians/gynecologists (SpOG), and subspecialists in oncology who have undergone standardized training to ensure a uniform understanding of the questionnaire and interview techniques.

Samples included are patients with VIA test negative was considered as clinically normal cervix, then undergone HPV DNA testing for further examination. We documented the age of the patient, age at sexual debut and menarche, smoking history, marital status, VIA test and HPV - DNA test results, and contraception usage. HPV DNA testing kit using HPV Xpress Matrix kit (PT KalGen DNA, Jakarta, Indonesia) and genotyping were conducted using PCR (SPF10-DEIA-LiPA25) in KalGen DNA diagnostics laboratory in Jakarta Indonesia. Highly satisfactory analytical sensitivity and specificity of this assay has been documented using a panel of WHO cloned HPV Plasmid DNA by the KalGen DNA diagnostics laboratory

Early sexual debut is defined as occurring before 18 years of age. Initiating sexual activity before 18 increases biological vulnerability to HPV infection due to cervical ectopy in adolescents, and has consistently been shown as an epidemiologic risk factor for persistent HPV infection, cervical intraepithelial neoplasia, and cervical cancer.[5,7,8]

The inclusion criteria were being married or sexually active subjects. The exclusion criteria were genital infection, had a cervical cancer or precancerous lesions, and pregnancy. The research flow of this study can be seen in Figure 1. This study was approved by University of Indonesia Review Board No. 0790/UN. F1/ ETIK/2018.

The data were processed using Statistical Product and Service Solutions (SPSS) software, version 27.0 for Windows. Association of early sexual debut with HPV infection was analyzed using the chi-square test, and the confounding variables were analyzed using logistic regression.

The unadjusted *p*-value was obtained from the model without controlling for confounding variables, while the adjusted *p*-value was calculated after adjusting for confounding variable. This adjustment was made to reduce bias and provide a more accurate estimation of the relationship between age at sexual debut and HPV infection.

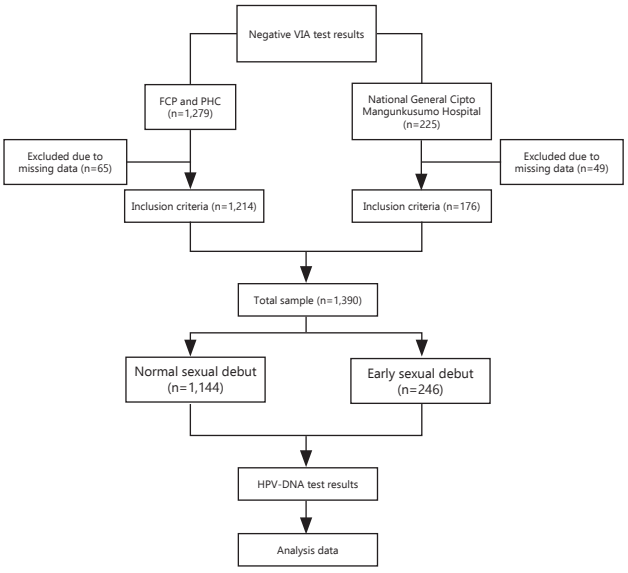

Figure 1. Flow diagram of the patients enrolled in this study.
Notes : FCP : Female Cancer Program; PHC : Public Health Care.

RESULTS

A total of 1,390 women met the inclusion criteria. The demographic characteristics are summarized in Table 1. The median age of participants was 41 years (IQR 34–75), with slightly more than half (51.4%) older than 40 years. The median age at sexual debut was 22 years (IQR 20–25), and 17.7% of women reported sexual debut at or before 18 years of age. The median menarche age, available for 545 participants, was 13 years. Most participants had never smoked (95%) and were married once (89.6%). Overall, 3.8% of subjects tested positive for HPV DNA. (Table1).

Table 1. Demographic Variables of the Women who Enrolled in this Study

Variables	Total n (%) or Median (IQR)
Sample Size (total)	1390 (100)
Age, Years, Median (IQR)	41.18 (34-75)
≤ 40	675 (48.6)
> 40	715 (51.4)
Sexual Debut, Years, Median (IQR)	22.32 (20-25)
≤ 18	246 (17.1)
> 18	1144 (82.3)
Smoking History	
Not Smoking	1321 (95)
Smoking	69 (5)
Marital Status	
Married Once	1246 (89.6)
Married more than once	77 (5.5)
Widow	67 (4.8)
HPV DNA Test Result	
Negative	1337 (96.2)
Positive	53 (3.8)
Contraception usage* (n = 1053)	
No History	536 (50.9)
Implant	21 (2.0)
Injected Contraception	185 (17.6)
Intrauterine Device (IUD)	93 (8.8)
Oral Contraception	161 (15.3)
Sterilization	57 (5.4)
Menarche, Years, Median (IQR)* (n = 545)	**13.38 (14-12)**
≤ 12	166 (30.5)
> 12	379 (69.5)

Notes.
*Data available for contraceptive usage n = 1053; and menarche n = 545 participants due to missing responses.

Table 2 shows the univariate and multivariate analyses of factors associated with HPV infection. Early sexual debut (≤18 years) was reported in 237 women (17.7%), including 20 who reported debut before age 14, but this factor was not significantly associated with HPV positivity (adjusted OR 0.981; 95% CI 0.491–1.882; p = 0.908). Likewise, no statistically significant associations were found for age group, smoking history, marital status, contraception use, or early menarche. Overall, none of the evaluated demographic or behavioral variables demonstrated a measurable association with HPV infection in this VIA-negative population. Among women aged ≤18 years, 96.3% were HPV-negative, while 3.6% were HPV-positive. Similarly, in the >18 years group, 96.1% were HPV-negative and 3.8% were HPV-positive. Overall, the proportion of HPV-positive cases is low in both age categories, and the percentages are nearly identical, indicating no notable difference in HPV positivity between younger (≤18) and older (>18) participants.

Table 2. Univariate and Multivariate Logistic Regression for Factors Associated with HPV DNA Result

Variables	HPV -, n (%)	HPV +, n (%)	Univariate Logistic Regression		Multivariate Logistic Regression (n=464)	
			Crude OR (95% CI)	*P-value (cs)*	Adjusted OR (95% CI)	*P-value (cs)*
All Subjects	1337 (96.2)	53 (3.8)				
Age, Years						
≤ 40	648 (46.6)	27 (50.9)	0.906 (0.523-1.568)	0.723		
> 40	689 (51.5)	26 (49.1)	Ref			
Sexual Debut Age, Years						
≤ 18	237 (17.7)	9 (17)	1.053 (0.507 - 2.187)	0.889		
> 18	1100 (82.3)	44 (83)	Ref			
Smoking History						
Not Smoking	1273 (95.2)	48 (90.6)	2.072 (0.798–5.382)	0.127	Ref	0.868
Smoking	64 (4.8)	5 (9.4)	Ref		0.881 (0.197-3.948)	
Marital Status						
Married Once	1196 (89.5)	50 (94.3)	Ref	0.247		
Married more than Once	74 (5.5)	3 (5.7)	0.171 (0.023-1.256)			
Widow	67 (5.0)	0 (0.0)				
Contraception Usage* (n = 1053)						
No History	512 (50.6)	24 (57.1)	Ref	0.961	Ref	0.382
Implant	20 (2.0)	1 (2.4)	0.770 (0.413-1.435)		1.404 (0.656-3.003)	
Injected Contraception	179 (17.7)	6 (14.3)				
Intrauterine Device (IUD)	89 (8.8)	4 (9.5)				
Oral Contraception	156 (15.4)	5 (11.9)				
Sterilization	55 (5.4)	2 (4.8)				
Menarche, Years* (n = 545)						
≤ 12	158 (30.9)	8 (24.2)	1.395 (0.616-3.160)	0.423	Ref	0.604
12	354 (69.1)	25 (75.8)	Ref		0.8 (0.345 - 1.856)	

Note: Age and sexual debut age could not be included in the multivariate logistic regression because these variables had no variability within the sample (constant values). Marital status was excluded from the model due to quasi-complete separation, as one category had zero HPV-positive cases, resulting in unstable estimates.

DISCUSSION

This study of 1,390 women with negative VIA results, we found no significant association between early sexual debut and HPV DNA positivity. Although 24% reported early initiation of sexual debut, HPV prevalence was similarly low in both the early and normative debut groups (3.6% vs. 3.8%), and adjusted ORs approached 1.0. Our results are consistent with previous study who reported no association between sexual debut before age 15 and the occurrence of HPV infection compared to sexual debut after the age of 24 years old,[9] other studies also report that age at first sexual debut often reflects underlying sexual behavior patterns particularly the lifetime number of partners rather than serving as an independent predictor of cervical HPV infection.[10] In contrast from findings in higher-risk referred populations such as the Brazilian study reporting an 87% prevalence of HPV infection was found, as well as that sexual debut at younger than 16 years old had a significant association with a positive HPV result (OR 4.41; 95% CI: 1.20 - 19.33; $P = 0.01$) due to different sample criteria; in their study, the sample was 198 patients referred with abnormal cytology results, while in our study, the sample was patients with clinically normal cervix.[10-12] The low HPV prevalence (3.8%) reduces statistical power to detect modest effects, Similar to other population-based screening studies, our participants were recruited from a healthier subset of the population. Because all women were VIA-negative and clinically normal, the study inherently sampled a low-risk group, which may reduce HPV prevalence and attenuate detectable associations between behavioral factors and HPV infection.[10]

Cervical cancer remains a substantial burden in LMICs and is almost universally associated with persistent HR-HPV infection.[13] Early sexual debut increases biological vulnerability because the adolescent transformation zone is more susceptible to HPV entry through microabrasions.[14,15] Studies suggest a 10–12-fold increase in cervical cancer risk when sexual debut occurs before age 18.[14] These findings highlight the importance of sexual and reproductive health

(SRH) interventions, as early sexual activity, early marriage, and SRH inequities contribute to adverse outcomes including cervical cancer.[16,17] Indonesia's context underscores this relevance. Despite policy efforts, early marriage remains common, with an estimated 46 million early marriages among adolescents over the past five years approximately 375 occurring daily.[6,18,19] This trend has direct implications for SDG 3 and SDG 5, which emphasize SRH access and the elimination of harmful practices such as child marriage.

Although early sexual debut was not significantly associated with HPV infection among women with normal cervical cytology in this study, the presence of HPV in this population reinforces the need for strong population-level prevention strategies. This suggests that preventive efforts should not rely solely on behavioral risk factors such as age at sexual debut but rather emphasize comprehensive HPV prevention strategies which has strongly supported by global guideline and long-term effectiveness data.[20-22] These include universal HPV vaccination prior to sexual initiation, continuous reproductive health education, and routine screening integrated into primary health care. These interventions are consistent with Indonesia's HPV and SRH programs and support both SDG 3.7 (universal access to reproductive health services) and SDG 5.6 (ensuring women's autonomy and access to SRH rights). Aligning prevention efforts with these goals promotes equitable access to HPV vaccination and screening, reduces future HPV-related disease burden, and accelerates progress toward cervical cancer elimination.[23]

This study has limitations. The small number of HPV-positive cases limited statistical precision, and self-reported data on sexual debut may introduce recall or social desirability bias. Use of a single HPV assay without genotyping may miss low-viral-load or non-16/18 infections.10 and restricting the sample to VIA-negative women limits generalizability.10 Future research should include larger and more diverse samples, incorporate HPV extended/full-genotyping, and collect partner-level data to better characterize transmission risk. Longitudinal designs across multiple locations would help differentiate HPV acquisition from persistence, and improved registry integration would strengthen evidence guiding cervical cancer prevention in Indonesia.

CONCLUSION

Early sexual debut was not significantly associated with HPV infection in women with a clinically normal cervix. Nevertheless, integration of HPV prevention, SRH education, and early screening initiatives remains pivotal to achieving SDG 3.7 and 5.6 targets in Indonesia.

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